Cardiovascular Revascularization Medicine 17 (2016) 355–361

Contents lists available at ScienceDirect

Cardiovascular Revascularization Medicine

Clinical

A randomized comparison of novel bioresorbable polymer sirolimus-eluting stent and durable polymer everolimus-eluting stent in patients with acute coronary syndromes: The CENTURY II high risk ACS substudy☆,☆☆,★

Victor A. Jiménez [a,*], Andrés Iñiguez [a], José A. Baz [a], Mariano Valdés [b], Alberto Ortiz [a], André Vuilliomenet [c], Vicente Mainar [d], Dariusz Dudek [e], Shmuel Banai [f], David Tüller [g], Jean-Louis Bonnet [h], Antonio De Miguel [a], Guillermo Bastos [a], William Wijns [i], Shigeru Saito [j]

[a] Interventional Cardiology Unit, Cardiology Department, Hospital Alvaro Cunqueiro, University Hospital of Vigo, Vigo, Spain
[b] Hospital Universitario V. Arrixaca, Murcia, Spain
[c] Kantonsspital Aarau, Aarau, Switzerland
[d] Department of Cardiology, University General Hospital of Alicante, Alicante, Spain
[e] Department of Interventional Cardiology, Jagiellonian University Medical College, Krakow, Poland
[f] Tel Aviv Sourasky Medical Centre, Tel Aviv, Israel
[g] Department of Cardiology, Stadtspital Triemli, Zürich, Switzerland
[h] Department of Cardiology, Hospital La Timone, Marseille, France
[i] Cardiovascular Center Aalst, OLV Hospital, Aalst, Belgium
[j] Department of Cardiology and Catheterization Laboratory, Shonan Kamakura General Hospital, Kamakura, Japan

ARTICLE INFO

Article history:
Received 30 March 2016
Accepted 8 April 2016

Keywords:
Acute coronary syndrome
bioresorbable polymer
drug-eluting stent

ABSTRACT

Background: To investigate clinical outcomes of percutaneous coronary intervention using a sirolimus-eluting stent with bioresorbable polymer, Ultimaster (BP-SES) compared with a permanent polymer everolimus-eluting stent, Xience (PP-EES) in patients with high risk (ST-segment elevation and non-ST-segment elevation myocardial infarction) acute coronary syndromes (ACS) enrolled in the CENTURY II trial.
Methods: CENTURY II is a prospective, multicenter, randomized, single blind, controlled trial comparing BP-SES and PP-EES, with primary endpoint of target lesion failure (TLF) at 9 month post-stent implantation. Out of 1123 patients enrolled in CENTURY II trial, 264 high risk ACS patients were included in this subgroup analysis, and the clinical outcomes including target lesion failure (TLF), target vessel failure (TVF), cardiac death, myocardial infarction, and stent thrombosis were evaluated at 24 months.
Results: The baseline clinical, angiographic and procedural characteristics were similar between two groups. At 24 months, TLF occurred in 6.3% of patients receiving a BP-SES and 6.5% of patients receiving a PP-EES (P = 0.95); TVF was 6.3% in patients receiving a BP-SES and 9.4% in patients receiving a PP-EES (P = 0.36). There were no significant differences in cardiac death, myocardial infarction and stent thrombosis rate.
Conclusions: BP-SES achieved similar safety and efficacy outcomes as PP-EES in this ACS subgroup of CENTURY II study, at 24-month follow-up. This finding is hypothesis-generating and needs to be confirmed in larger trials with longer follow-up.

1. Introduction

Late stent thrombosis (ST) and late stent restenosis have been associated with a chronic inflammatory vessel response induced by components of the permanent polymer matrix [1]. This inflammatory process results in delayed arterial healing and hypersensitivity reactions, and has been demonstrated in histopathological studies of first-generation drug-eluting stents (DES) [1]. The availability and use of

☆ Conflict of interest: W.W. reports institutional research grants from Abbott Vascular and Terumo; shareholder and non-executive board member of Cardio3BioSciences and Genae Inc. The rest of authors have no potential conflict of interest to disclose.
☆☆ Clinical trial registration URL:https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr.cgi?function=brows&action=brows&type=summary&recptno=R000008202&language=E
★ Unique Identifier: UMIN000006940
* Corresponding author at: Cardiovascular Research Unit, Cardiology Department, Hospital Alvaro Cunqueiro, University Hospital of Vigo, Estrada Clara Campoamor 341, Planta 4, Vela B, 36312, Vigo, Spain. Tel.: +34986825564.
E-mail address: victor.alfonso.jimenez.diaz@sergas.es (V.A. Jiménez).

http://dx.doi.org/10.1016/j.carrev.2016.04.001

DES with a bioresorbable polymer (BP) could overcome these drawbacks, providing safety and benefits in different clinical settings, including stable coronary artery disease (CAD) and acute coronary syndromes (ACS).

The safety and effectiveness of BP-based DES over bare metal stents [2] (BMS) and first-generation DES [3] has been proven previously in reducing the risk of very late ST and restenosis [4]. Patients with ACS constitute a challenging subset with poorer outcomes after percutaneous coronary interventions (PCI) as compared to stable CAD, with an increased risk of ST and reinfarction. Therefore, the potential benefits of a BP-based DES in patients with ACS are important, but its efficacy and safety remains to be confirmed.

In the CENTURY II (Clinical Evaluation of New Terumo Drug-Eluting Coronary Stent System in the Treatment of Patients with Coronary Artery Disease) trial, a sirolimus-eluting stent with BP, Ultimaster (BP-SES) showed safety and efficacy profiles similar to permanent polymer everolimus-eluting stent (PP-EES) at 9-month follow-up [5].

To date, there are few data regarding the comparison of the current gold-standard generation DES with the BP-SES in patients with high-risk ACS, including ST-segment elevation myocardial infarction (STEMI) and non-STEMI patients (NSTEMI). We present the analysis of a subgroup of patients with high risk ACS treated with BP-SES or PP-EES in the CENTURY II trial.

2. Methods

2.1. Study design

The CENTURY II study design and study devices have been described in detail in a previous publication [5]. In brief, CENTURY II is a prospective, multicenter, randomized (1:1), single blind, controlled, non-inferiority, two-arm trial of BP-SES (Ultimaster DES, Terumo Corporation, Tokyo, Japan) and PP-EES (Xience DES, Abbott Vascular, Santa Clara, California, USA). Patients aged ≥18 years, with clinical evidence of ischemic heart disease and/or a positive functional study, good candidates for PCI using DES and acceptable candidates for CABG with reference vessel diameter between ≥2.5 mm and ≤4.0 mm were included in the study. A complete description of exclusion criteria is listed in Supplementary Appendix.

The global study included 1123 patients in 58 participating centers from Europe, Japan, and Korea, from February 2012 to January 2013. The current study included all patients with high-risk ACS (STEMI and NSTEMI). This ACS subgroup was prespecified in the protocol. Except for Japan (15 sites), and South Korea (1 site), all European centers (42 sites in 11 European countries) enrolled patients with high risk ACS (complete list in supplementary appendix). The study was approved by the institutional review committee at each participating center and all patients provided written informed consent.

2.2. Procedures

PCI were performed according to standard hospital practice. Patients were randomly assigned (1:1) to receive either BP-SES or PP-EES. Randomization of patients was stratified by general inclusion and exclusion criteria and balanced for diabetes mellitus, ACS (STEMI and NSTEMI) and multivessel disease. All further procedures (lesion pre-dilation, stenting or post-stenting dilation, usage of imaging modalities for result optimization or glycoprotein (GP) IIb/IIIa inhibitors) were left at operator's discretion. Dual antiplatelet therapy (DAPT) prescription was according to hospital practice in all patients, with a duration for at least 6 months as per protocol recommendation. DAPT beyond 6 months was at the discretion of the treating physician considering prevailing guidelines [6]. All patients were to be followed up at 1, 4, and 9 months and yearly up to 5 years.

2.3. Endpoints and definitions

The primary endpoint of CENTURY II study was target lesion failure (TLF), a device-oriented composite endpoint (cardiac death, MI not clearly attributable to a non-target vessel, and clinically driven target lesion revascularization [TLR]) at 9 months post-stent implantation. Secondary endpoints were: (i) rate of target vessel failure (TVF) defined as composite of cardiac death and MI not clearly attributable to a non-target vessel, and clinically driven target vessel revascularization (TVR); (ii) patient-oriented composite endpoint (POCE) composed of all deaths, all MI and all coronary revascularizations; (iii) rate of TLR, TVR, ST, cardiac death, and MI; (iv) composite of cardiac death and MI; and (v) rate of bleeding and vascular complications according to Bleeding Academic Research Consortium (BARC) definitions [7]. The endpoints were defined as per Academic Research Consortium (ARC) recommendations [8].

2.4. Angiographic analysis

All angiograms were assessed by an independent core laboratory (K.I.C. Co. Ltd, Kanagawa, Japan) using dedicated software (qAngio XA ver. 7.1, Medis, the Netherlands). Main angiographic parameters at

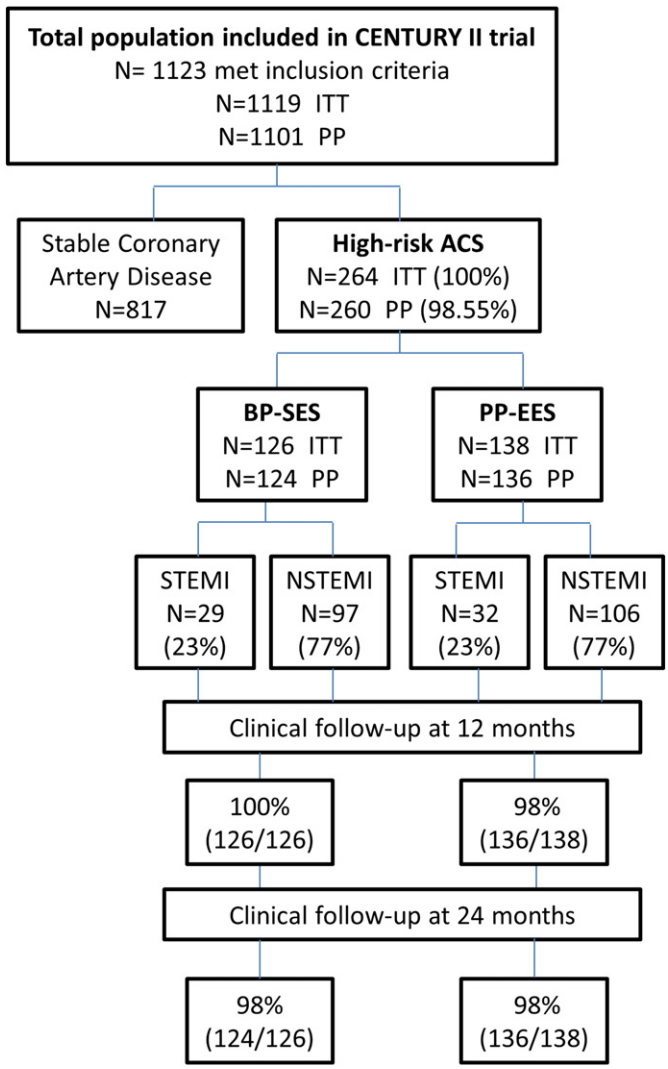

Fig. 1. Flow chart of CENTURY II ACS substudy ITT = intention to treat; PP = per-protocol; ACS = acute coronary syndromes; BP-SES = bioresorbable polymer sirolimus-eluting stent; PP-EES = permanent polymer everolimus-eluting stent; STEMI = ST-segment elevation myocardial; NSTEMI = non-ST segment elevation myocardial.

Table 1
Baseline patient characteristics.

	Total HR-ACS n = 264	BP-SES n = 126	PP-EES n = 138	P value
Age, (years)	63.7 ± 11.3	63.1 ± 11.3	64.3 ± 11.4	0.45
Male gender, % (n)	82.2% (217)	79.3% (100)	84.7% (117)	0.25
Clinical presentation				
STEMI, % (n)	23.1% (61)	23.0% (29)	23.1% (32)	0.97
NSTEMI, % (n)	76.8% (203)	76.9% (97)	76.8% (106)	0.97
Diabetes mellitus	23.4% (62)	25.4% (32)	21.7% (30)	0.48
Insulin-treated, % (n)	4.1% (11)	5.5% (7)	2.8% (4)	0.38
Hypertension, % (n)	58.0% (152)	58.8% (73)	57.2% (79)	0.79
Dyslipidemia, % (n)	51.9% (133)	48.3% (59)	55.2% (74)	0.27
Current smoking, % (n)	36.5% (95)	39.0% (48)	34.3% (47)	0.43
Previous MI, % (n)	33.3% (88)	31.7% (40)	34.7% (48)	0.60
Previous PCI, % (n)	21.5% (57)	21.4% (27)	21.7% (30)	0.95
Multivessel disease	50.3% (133)	47.6% (60)	52.9% (73)	0.39
LVEF, %	56.3 ± 11.3	55.7 ± 11.5	56.9 ± 11.1	0.63
Killip classification				0.44
Class 1, % (n)	85.2% (52)	82.7% (24)	87.5% (28)	
Class 2, % (n)	13.1% (8)	13.7% (4)	12.5% (4)	
Class 3–4, % (n)	1.6% (1)	3.4% (1)	0.0% (0)	
Complexity of CAD				
≥1 lesion >20mm, % (n)	46.7% (123)	50.0% (63)	43.8% (60)	0.31
≥1 bifurcation, % (n)	12.5% (33)	11.9% (15)	13.0% (18)	0.78
Left main, % (n)	1.5% (4)	0.7% (1)	2.1% (3)	0.36
Total occlusion, % (n)	14.3% (38)	11.9% (15)	16.6% (23)	0.27
Syntax score	9.7 ± 6.5	9.2 ± 6.0	10.3 ± 6.9	0.25

Data are mean ± SD or %. HR-ACS: high risk acute coronary syndromes; BP-SES: bioresorbable polymer sirolimus-eluting stent (s); PP-EES: permanent polymer everolimus-eluting stent(s); STEMI: ST-segment elevation myocardial infarction; NSTEMI: non-ST-segment elevation myocardial infarction; CAD: coronary artery disease; MI: myocardial infarction; PCI: percutaneous coronary intervention; LVEF, left ventricle ejection fraction.

baseline were minimum lumen diameter (MLD) before and after procedure, percentage diameter stenosis (DS%), and acute gain (defined as the change in MLD from baseline to the final procedural angiogram).

2.5. Statistical analysis

The statistical analysis plan has previously been published [5]. The CENTURY II randomized trial was powered for non-inferiority of BP-SES compared with PP-EES for the primary endpoint of 9-month TLF. The Kaplan–Meier method was used to estimate event rates for time-to event outcomes, and data were compared with the log-rank test. All analyses were carried out using the SAS software, version 9.1 (SAS Institute, Inc., Cary, NC, USA).

3. Results

3.1. Patient characteristics

Out of 1123 patients enrolled in CENTURY II, 264 were high risk ACS patients which were randomly assigned to receive BP-SES (n = 126) or PP-EES (n = 138). Mean age was 63.7 years, 82.2% were male, and 23.4% were diabetic patients. In this subgroup, 23.1% were STEMI patients while 76.9% were NSTEMI patients (Fig. 1). Baseline demographic and clinical characteristics did not significantly differ between two study groups (Tables 1 and 2).

3.2. Angiographic results

A total of 354 lesions (159 with BP-SES and 195 with PP-EES) were treated with a mean of 1.7 stents implanted per patient. Treated vessel was the left anterior descending (LAD) coronary artery in more than 40% of cases with two thirds of the procedures performed via transradial approach. More than 75% of treated lesions displayed complex features (B2 or C) as rated by the ACC/AHA. Details of procedural and lesions characteristics are shown in Tables 2 and 3.

Table 2
Baseline lesion and procedural characteristics.

	Total HR-ACS N = 264 Nlesion = 371	BP-SES N = 126 Nlesion = 166	PP-EES N = 138 Nlesion = 205	P value
Number of stents implanted per patient, n	1.65 ± 0.90	1.55 ± 0.77	1.75 ± 1.00	0.24
Number of stents implanted per lesion, n	1.18 ± 0.44	1.17 ± 0.44	1.19 ± 0.44	0.61
Stent length per patient, mm	31.52 ± 19.11	30.31 ± 17.50	32.62 ± 20.45	0.74
Stent length per lesion, mm	22.65 ± 10.14	22.96 ± 10.49	22.39 ± 9.87	0.34
Lesion location (target vessel)				0.72
LAD, % (n)	40.16% (149)	42.77% (71)	38.05% (78)	
LCX, % (n)	29.92% (111)	29.52% (49)	30.24% (62)	
RCA, % (n)	28.57% (106)	27.11% (45)	29.76% (61)	
LM, % (n)	1.08% (4)	0.60% (1)	1.46% (3)	
Graft, % (n)	0.27% (1)	0.0% (0)	0.49% (1)	
Number of vessels treated per patient, n	1.23 ± 0.47	1.17 ± 0.39	1.28 ± 0.53	0.06
Number of lesions treated per patient, n	1.41 ± 0.66	1.32 ± 0.59	1.49 ± 0.72	0.03
Vascular access site				0.81
Radial, % (n)	72.35% (191)	73.02% (92)	71.74% (99)	
Femoral,% (n)	27.65% (73)	26.98% (34)	28.26% (39)	
Complete revascularization	67.05% (177)	70.63% (89)	63.77% (88)	
Preprocedural TIMI flow grade				0.23
0–1, % (n)	13.59 % (48/353)	11.39% (18/158)	15.39% (30/195)	
2, % (n)	18.13% (64/353)	18.99% (30/158)	17.44% (34/195)	
3, % (n)	68.27% (241/353)	69.62% (110/158)	67.18% (131/195)	
ACC/AHA lesion classification				0.49
A, % (n)	4.24% (15/354)	5.03% (8/159)	3.59% (7/195)	
B1, % (n)	15.54% (55/354)	13.84% (22/159)	16.92% (33/195)	
B2, % (n)	50.00% (177/354)	47.80% (76/159)	51.79% (101/195)	
C, % (n)	30.23% (107/354)	33.33% (53/159)	27.69% (54/195)	
Thrombus present, % (n)	11.02% (39/354)	10.06% (16/159)	11.79% (23/195)	0.60
Calcification				0.98
None/mild, % (n)	87.57% (310/354)	86.16% (137/159)	88.72% (173/195)	
Moderate, % (n)	8.76% (31/354)	9.43% (15/159)	8.21% (16/195)	
Severe, % (n)	3.67% (13/354)	4.40% (7/159)	3.08% (6/195)	
Ostial lesion, % (n)	5.08% (18/354)	3.14% (5/159)	6.67% (13/195)	0.13

Data are mean ± SD or %. LAD, left anterior descending; LCX, left circumflex; RCA, right coronary artery; LM, left main; TIMI, thrombolysis in myocardial infarction; ACC/AHA, American College of Cardiology/American Heart Association.

3.3. Clinical outcomes

Follow-up at 24 months was available in 98% (124/126 in BP-SES group and 136/138 in PP-EES group) of the patients (Fig. 1). TLF occurred in 6.3% (8/126) of patients receiving a BP-SES and 6.5% (9/138) of patients receiving a PP-EES (P = 0.95) (Table 4). Individual components of the TLF showed comparable rates of cardiac death (0.0% in BP-SES and 2.1% in PP-EES; P = 0.10), target vessel MI (0.7% in BP-SES and 3.6% in PP-EES; P = 0.12), and clinically driven TLR (4.8% BP-SES and 3.6% PP-EES; P = 0.64) at 24-month follow-up. TVF occurred in 6.3% (8/126) of patients receiving a BP-SES and 9.4% (13/138) of patients receiving a PP-EES (P = 0.36) (Table 4). POCE at 24-month post-stent implantation was 11.9% (15/126) of patients receiving a BP-SES and 14.5% (20/138) of patients receiving a PP-EES (P = 0.58) (Table 4). ST (definite + probable) occurred in 2 patients (1.59%) in the BP-SES, and in one patient (0.72%) in the PP-EES group (P = 0.51), all as subacute events (Table 5). At 12 and 24 months follow-up, 60% and 19% of patients continued with DAPT, respectively, with no significant differences between groups. Since the polymer of the BP-SES completely degrades over 3 to 4 months, we performed further landmark analysis to compare the clinical events occurring within the first 4 months and beyond the first 4 months. Landmark Kaplan–Meier analysis for TLF, TVF, and POCE within 4 months and up to 24 months is presented in Figs. 2–4.

Table 3
QCA lesion characteristics.

	Total HR-ACS n = 264	BP-SES n = 126	PP-EES n = 138	P value
Number of lesions analyzed	354	159	195	
Lesion length, mm	19.97 ± 10.07	21.04 ± 10.96	19.08 ± 9.20	0.14
Pre-procedure				
RVD, mm	2.65 ± 0.59	2.68 ± 0.56	2.62 ± 0.62	0.29
MLD, mm	0.73 ± 0.42	0.75 ± 0.40	0.71 ± 0.44	0.52
% Diameter stenosis, %	72.29 ± 14.54	72.09 ± 13.36	72.45 ± 15.47	0.64
Post-procedure				
MLD, mm				
In-stent	2.51 ± 0.47	2.53 ± 0.46	2.49 ± 0.49	0.41
In-segment	2.14 ± 0.62	2.19 ± 0.60	2.11 ± 0.63	0.26
% Diameter stenosis, %				
In-stent	12.46 ± 6.40	12.58 ± 6.30	12.37 ± 6.51	0.74
In-segment	23.90 ± 11.77	23.40 ± 11.68	24.31 ± 11.86	0.33
Acute gain, mm				
In-stent	1.79 ± 0.54	1.78 ± 0.50	1.79 ± 0.56	0.91
In-segment	1.42 ± 0.65	1.44 ± 0.59	1.40 ± 0.69	0.42

Data are mean ± SD. QCA, quantitative coronary angiography; RVD, reference vessel diameter; MLD, minimal luminal diameter.

4. Discussion

This study reported the 24-month clinical outcomes of new-generation BP-SES compared with PP-EES in ACS patients from the CENTURY II trial. The Ultimaster BP-SES was similar to Xience PP-EES with respect to TLF in patients with ACS, including STEMI and NSTEMI. The good clinical performance and safety of Ultimaster BP-SES was particularly reflected in the low rates of cardiac death and MI achieved up to 24 months, comparable with the PP-EES group, as well as in the non-significant differences obtained regarding POCE, with a similar frequency of ST among BP-SES and PP-EES-treated patients, and without any late event. The BP-SES matched the clinical outcomes of the PP-EES, one of the safest and most effective DES currently available. This is reassuring since PP-EES have previously been shown to improve outcomes and reduce the risk of mortality, MI, ST, and repeat revascularization as compared to early-generation DES in challenging populations including ACS patients [9,10].

4.1. Previous studies with BP-DES vs. PP-DES in ACS

Few data exist regarding the use of DES with biodegradable polymer in patients with ACS. In the subgroup of ACS patients of the COMPARE II trial [11], the biodegradable polymer biolimus-eluting stent was non-inferior to durable fluoropolymer-based everolimus-eluting stent with regards to the primary endpoint, a composite of safety (cardiac death and non-fatal MI) and efficacy (clinically indicated TVR) at 12 months (5.2% in the biolimus-eluting stent group vs. 4.8% in the everolimus-eluting stent group; $P_{non\text{-}inferiority} < 0.0001$). Definite ST was similar in both groups (0.7% vs. 0.4%, P = 0.38).

In the pooled individual patient-level analysis from three randomized clinical trials [12] (ISAR-TEST-3, ISAR-TEST-4 and LEADERS) comparing outcomes from BP-DES with PP-DES in 497 STEMI patients at four years, the primary endpoint (comprised of cardiac death, MI, or TLR), was significantly reduced following treatment with BP-DES (14.2% vs. 23%; P = 0.01) driven by reduced TLR (7.4% vs. 13.1%; P = 0.04). In addition, trends toward reduction for cardiac death or MI (9.5% vs. 15.0%; P = 0.07) and definite or probable ST (3.6% vs. 7.1%; P = 0.09) were reported in the BP-DES group.

In the prespecified subgroup of patients with STEMI of the BIOSCIENCE (Ultrathin strut biodegradable polymer sirolimus-eluting stent versus durable polymer everolimus-eluting stent for percutaneous coronary revascularization) trial [13], 407 (19%) STEMI patients were included. Ultrathin strut biodegradable polymer stent was associated with a lower risk of TLF (3.3%) than with durable polymer stent (8.7%; P = 0.024) at 12 months.

These reports from subpopulation analysis are comparable with our results, however prospective randomized clinical trials on a large scale are needed, specifically those designed for this patient population.

4.2. Potential benefit of BP-DES in ACS

ACS is constituted by a heterogeneous group of patients that differs greatly from the population of patients with stable coronary disease, showing a higher risk of developing subsequent coronary events such as ST and reinfarction. Previous studies using intravascular imaging assessment after DES implantation in STEMI patients have shown a higher proportion of uncovered struts and incomplete stent apposition at follow-up, potentially due to an adverse vessel remodeling and late-acquired incomplete stent apposition, a phenomenon related to hypersensitivity and attenuation of the vessel's healing processes induced by DES polymer [14].

Table 4
Clinical outcomes at 24 months.

	Total HR-ACS n = 264	BP-SES n = 126	PP-EES n = 138	P value
All cause death, % (n)	2.2% (6)	1.5% (2)	2.9% (4)	0.48
Cardiac death, % (n)	1.1% (3)	0.0% (0)	2.1% (3)	0.10
All MI, % (n)	3.4% (9)	2.3% (3)	4.3% (6)	0.38
Target vessel MI, % (n)	2.2% (6)	0.7% (1)	3.6% (5)	0.12
All revascularizations, % (n)	10.2% (27)	8.7% (11)	11.5% (16)	0.44
Clinically indicated revascularizations, % (n)	7.5% (20)	7.1% (9)	7.9% (11)	0.80
TLR, % (n)	4.5% (12)	5.5% (7)	3.6% (5)	0.45
TV non-TLR revascularization, % (n)	3.7% (10)	2.3% (3)	5.0% (7)	0.25
TVR, % (n)	6.4% (17)	5.5% (7)	7.2% (10)	0.58
NTVR, % (n)	5.6% (15)	5.5% (7)	5.8% (8)	0. 93
Composite endpoints				
TLF, % (n)	6.4% (17)	6.3% (8)	6.5% (9)	0.95
TVF, % (n)	7.9% (21)	6.3% (8)	9.4% (13)	0.36
Cardiac death and MI, % (n)	4.1% (11)	2.3% (3)	5.8% (8)	0.17
All death, MI, and revascularization, % (n)	13.2% (35)	11.9% (15)	14.5% (20)	0.54

TLR, target lesion revascularization; TV, target vessel; TVR, target vessel revascularization; NTVR, non-target vessel revascularization; TLF, target lesion failure; TVF, target-vessel failure.

Table 5
Antiplatelet treatment, bleeding and stent thrombosis.

	Total HR-ACS n = 264	BP-SES n = 126	PP-EES n = 138	P value
Preprocedural antiplatelet medications				
Aspirin, % (n)	83.3% (220)	84.9% (107)	81.8% (113)	0.51
Clopidogrel, % (n)	46.5% (123)	48.4% (61)	44.9% (62)	0.57
Prasugrel, % (n)	10.9% (29)	9.5% (12)	12.3% (17)	0.47
Ticagrelor, % (n)	15.5% (41)	14.2% (18)	16.6% (23)	0.59
DAPT, % (n)	72.7% (192)	71.4% (90)	73.9% (102)	0.65
Stent thrombosis (definitive + probable) at 24-month,% (n)				
Acute, % (n)	0.0% (0)	0.0% (0)	0.0% (0)	1.0
Subacute, % (n)	1.1% (3)	1.5% (2)	0.7% (1)	0.51
Late/very late, % (n)	0.0% (0)	0.0% (0)	0.0% (0)	1.0
DAPT use at 12 months, % (n)	60.0% (146)	62.0% (72)	58.2% (74)	0.55
DAPT use at 24 months, % (n)	19.2% (49)	21.3% (26)	17.4% (23)	0.43
Any bleeding 12 months, % (n)	9.4% (25)	8.7% (11)	10.1% (14)	0.56
Any bleeding 24 months, % (n)	11.7% (31)	11.9% (15)	11.5% (16)	0.93

DAPT, dual antiplatelet therapy.

At the same time, the persistent inflammation and high platelet reactivity displayed by patients with ACS, and the delayed endothelialization of PP-DES compared to BMS, favor the use of DAPT for long time, even in populations with high concurrent bleeding risk. Therefore, the possibility of having a device that offers the advantages of DES in terms of reduction of repeat revascularizations and restenosis combined with the safety of BMS regarding the risk of late thrombosis is highly attractive, moreover adding the benefit of current and more efficient antiplatelet therapies, could encouraged a possible reduction in DAPT duration in ACS patients with high bleeding risk.

At present, there is no specific recommendation for DAPT duration after BP-DES implantation. Consequently, it should not differ from that of a PP-DES in current clinical practice until we have more data from a larger patient population with longer term follow-up to confirm this theory.

The good performance obtained regarding safety and efficacy by the BP-SES in this study is encouraging and could be explained, in part, by its bioresorbable polymer, abluminal coating, thinner cobalt-chromium stent platform (80 μm) with an open-cell design for easy access to a side branch and conformability to the vessel wall, the absence of drug and polymer on blood contacting surface, and the short polymer degradation time allow rapid drug elution (three to four months), which might promote early endothelialization. No significant differences were observed during or beyond the 4-month polymer degradation period of Ultimaster BP-SES compared with Xience PP-EES, regarding TLF, TVF, and POCE (Figs. 2–4). Also, previous studies have demonstrated on OCT at 9-month follow-up the lower frequency of uncovered struts with a BP-DES compared with a PP-DES [15].

Important factors implied in ST and restenosis such as localized hypersensitivity reaction to the polymer or its carriers causing delayed healing, and stent coverage by non-functional endothelium are avoided by the use of a BP [14]. In the CENTURY study, the Ultimaster BP-SES showed almost complete stent endothelialization after 6 months of implantation, with absence of vessel remodeling and unchanged vessel volume peri-stent by IVUS and OCT analysis [16].

Whether the degree of strut coverage and lack of malapposition (evaluated by OCT) are sufficient parameters to safely discontinue DAPT without the risk of ST is currently not known and needs to be properly assessed in a prospective clinical trial. It also remains to be demonstrated whether the use of new technologies as BP with thin-strut stent platforms, seeking to achieve a more rapid re-endothelialization and an improved healing pattern, will overcome the small drawbacks of current DES-generation in terms of ST and stent restenosis. Moreover, these benefits should be compared with a variety of new DES technologies with ultrathin platform, DES without polymer, and the bioresorbable scaffolds in ACS patients.

4.3. Limitations

This is a pre-specified subgroup analysis of a large randomized, prospective, multicenter study. The CENTURY II study reached its primary endpoint by showing non-inferiority of TLF at 9 months in patients treated with BP-SES comparing with patients treated with PP-EES, but was not powered to address individual components of efficacy or safety. This sample size of this ACS subgroup is small and events rates were low, therefore does not have sufficient power to draw definite conclusions from this subgroup analysis. Our findings should be considered only as hypothesis-generating. The study patients were enrolled from high-volume centers in 11 European countries. Therefore, geographical variations in PCI practice outside Europe or in lower-volume centers cannot be excluded. CENTURY II had limited exclusion criteria (Appendix), and this subgroup included ACS patients with complex anatomical disease. However, that might not fully represent the real features of the population treated in our routine clinical practice.

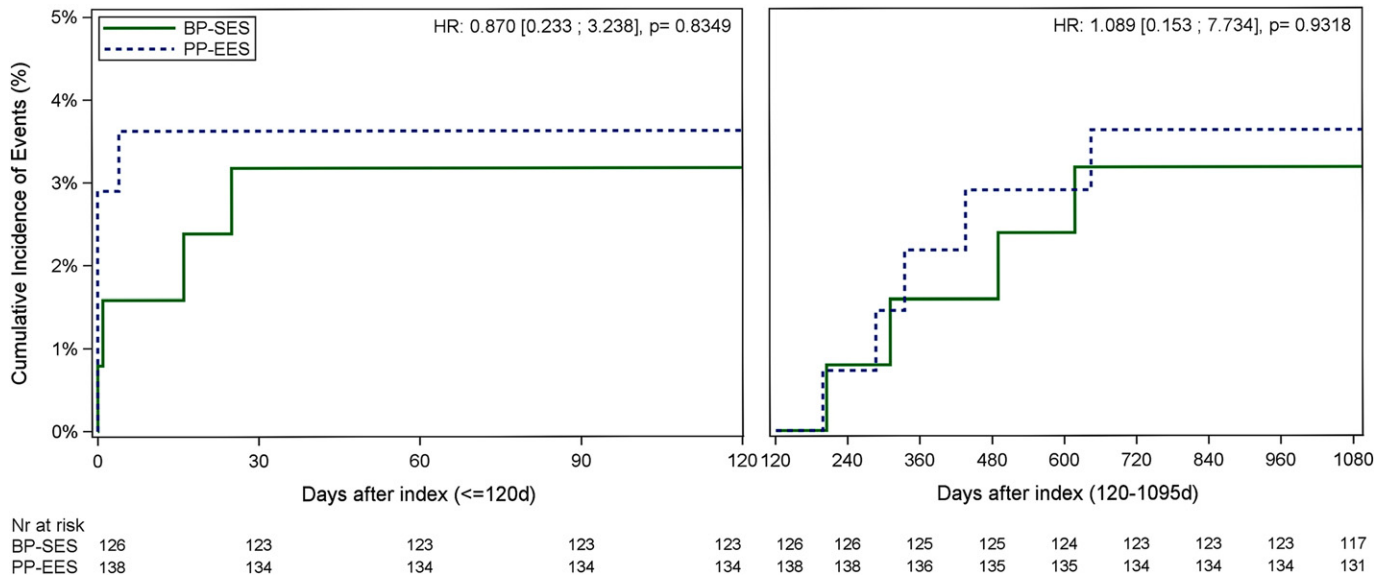

Fig. 2. Landmark Kaplan–Meier analysis of target lesion failure (TLF) BP-SES = bioresorbable polymer sirolimus-eluting stent; PP-EES = permanent polymer everolimus-eluting stent; TLF = target lesion failure; HR = hazard ratio.

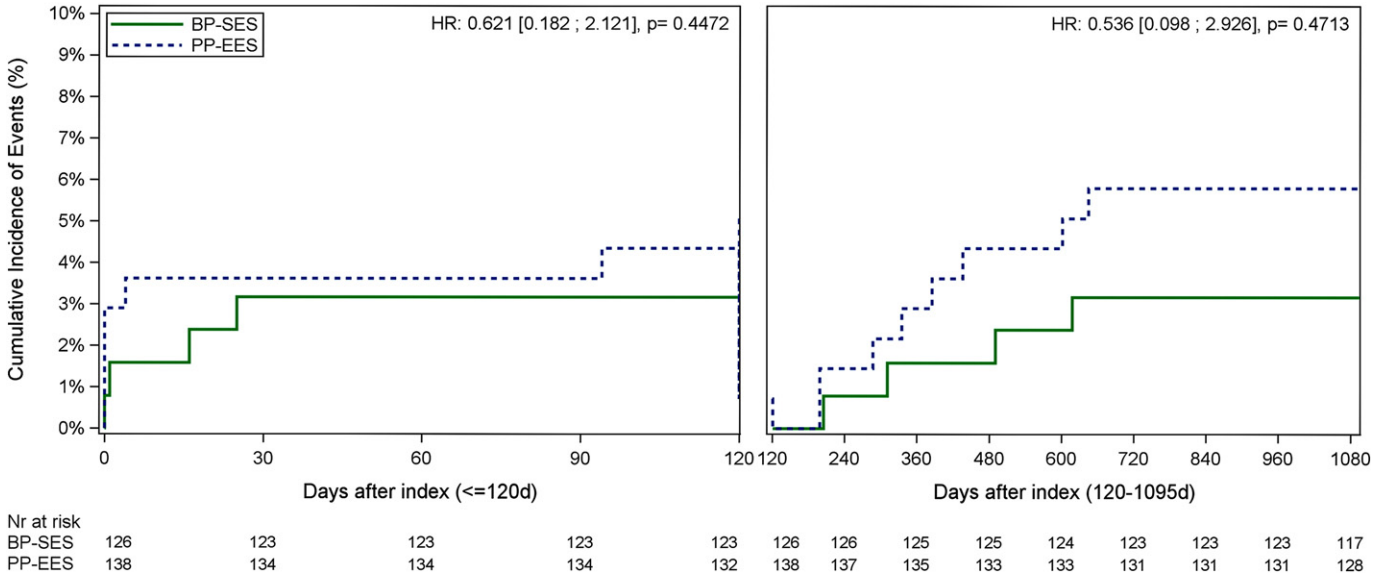

Fig. 3. Landmark Kaplan–Meier analysis of target vessel failure (TVF) BP-SES = bioresorbable polymer sirolimus-eluting stent; PP-EES = permanent polymer everolimus-eluting stent; TVF = target vessel failure; HR = hazard ratio.

5. Conclusions

Our findings suggest that the use of Ultimaster BP-SES in patients with high risk ACS, including STEMI, is non-inferior to the Xience PP-EES regarding composite clinical endpoints of cardiac death, TV-MI or TLR at 24 months and is associated with a favorable safety profile as evidenced by similar rates of ST throughout 2 years. The latter finding is hypothesis-generating and requires validation in appropriately designed studies.

Acknowledgement

CENTURY II study was funded by Terumo Corporation, Tokyo, Japan.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.carrev.2016.04.001.

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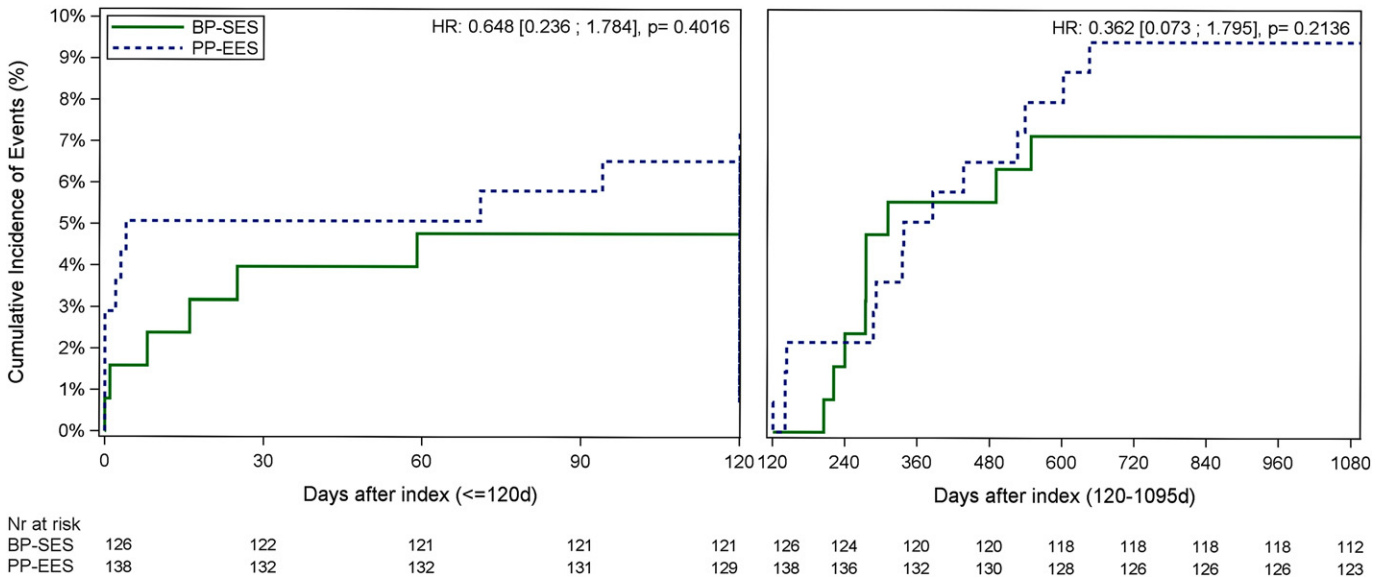

Fig. 4. Landmark Kaplan–Meier analysis of patient-oriented composite endpoint (POCE) BP-SES = bioresorbable polymer sirolimus-eluting stent; PP-EES = permanent polymer everolimus-eluting stent; POCE = patient-oriented composite endpoint (composed of all deaths, myocardial infarction and coronary revascularizations); HR = hazard ratio.

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